

1 What is claimed is:

2 1. A method of determining the sequence of a nucleic acid, comprising steps of:

3 (a) hybridizing an oligonucleotide to a single stranded DNA, wherein
4 the oligonucleotide is complementary to at least a portion of the single
5 stranded DNA;

6 (b) providing a DNA polymerase and four deoxynucleotide
7 triphosphates (dNTPs) comprising dATP, dGTP, dCTP, and dTTP,
8 wherein each dNTP is 3'-end labeled with a cleavable tag (cdNTP) that
9 distinguishes it from the other cdNTPs;

10 (c) extending the single stranded DNA hybridized to the
11 oligonucleotide by one complementary end-labeled cdNTP in a
12 polymerase extension reaction, wherein the tag on the extended cdNTP
13 blocks further extension by the DNA polymerase;

14 (d) cleaving the tag from the complementary cdNTP; and

15 (e) detecting the tag, thereby identifying the complementary dNTP.

16 2. The method of claim 1, further comprising the step of removing excess
17 cdNTPs that are not extended onto the single stranded DNA.

18 3. The method of claim 1, further comprising the step of repeating steps (a)
19 through (e) on the sample of single stranded DNA.

- 1 4. The method of claim 1, wherein the cleavable tags are cleavable by chemical
2 cleavage.
- 3 5. The method of claim 4, wherein the cleavable tags are acid cleavable tags.
- 4 6. The method of claim 4, wherein the cleavable tags are base cleavable.
- 5 7. The method of claim 1, wherein the tags are photocleavable.
- 6 8. The method of claim 1, wherein the tag is a fluorescent tag.
- 7 9. The method of claim 1, wherein the tag is a mass tag.
- 8 10. A method of determining the sequence of a nucleic acid, comprising steps of:
- 9 (a) hybridizing a complementary oligonucleotide to a single stranded DNA,
10 wherein the oligonucleotide is 3'-end labeled with one or more cleavable tags
11 that distinguishes it from other oligonucleotides;
- 12 (b) cleaving the one or more tags from the ligated complementary
13 oligonucleotide; and
- 14 (c) detecting the one or more tags.
- 15 11. The method of claim 10, wherein the hybridizing of the complementary
16 oligonucleotide occurs adjacent to a primer.
- 17 12. The method of claim 11, further comprising ligating the hybridized
18 oligonucleotide to the primer.

- 1 13. The method of claim 12, further comprising the step of removing excess
2 oligonucleotides that are not ligated onto the single stranded DNA.
- 3 14. The method of claim 12, further comprising the step of repeating steps (a)
4 through (c) on the single stranded DNA.
- 5 15. The method of claim 10, wherein one or more tags are cleaved by chemical
6 cleavage.
- 7 16. The method of claim 15, wherein the cleavable tags are acid cleavable tags.
- 8 17. The method of claim 15, wherein the cleavable tags are base cleavable.
- 9 18. The method of claim 10, wherein the tags are photocleavable.
- 10 19. The method of claim 10, wherein the tag is a fluorescent tag.
- 11 20. The method of claim 10, wherein the tag is a mass tag.

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